

**UNITED STATES DEPARTMENT OF COMMERCE****Patent and Trademark Office**

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/716,732	11/20/00	GHOSH	R 97,022-N2

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EXAMINER	
COOK, L	
ART UNIT	PAPER NUMBER

1641

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DATE MAILED: 07/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/716,732	GHOSH ET AL.
Examiner	Art Unit	
Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 20 November 2000.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1 and 18 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1 ^{and 18} is/are rejected.

7) Claim(s) 18 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. ____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) Other: _____

DETAILED ACTION

Preliminary Amendment Entry

1. Applicant's preliminary Amendment-B filed 11/20/00 is acknowledged. Claims 2-17 and 19-20 were canceled without prejudice. Currently claims 1 and 18 are pending and under consideration.

Priority

2. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). It is noted that this application appears to claim subject matter disclosed in prior copending Application Nos. (08/810,983 -filed 2/27/97 now U.S. Patent #5,989,835). A reference to the prior applications must be inserted as the first sentence of the specification of this application if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). Also, the current status of all nonprovisional parent applications referenced should be included.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on PTO-1449 has cited the references they have not been considered.

Drawings

4. The drawings in this application are objected to by the Draftsperson as informal. Any drawing corrections requested, but not made in the prior application should be repeated in this application if such changes are still desired. If the drawings were changed and approved during the prosecution of the prior application, a petition may be filed under 37 CFR 1.182 requesting the transfer of such drawings, provided the parent application has been abandoned. However, a copy of the drawings as originally filed must be included in the 37 CFR 1.60 application papers to indicate the original content.

Oath/Declaration

5. A new oath or declaration is required because:

I. The declaration is directed to application number 09/632,552-filed 8/4/00. However, the instant application is for U.S. application number 09/716,732-filed 11/20/00.

II. It does not identify the post office address of each inventor. A post office address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The post office address should include the ZIP Code designation. The residence of the third inventor is listed as a P.O. Box with the Zip Code. Please correct residence and add Zip to Post Office address.

The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Specification

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. The disclosure is objected to because of the following informalities: The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. Examples are on pages 58 and 60. New application papers with lines double spaced on good quality paper are required. 37 CFR 1.52(b) requires that the pages of the specification including claims and abstract must be numbered consecutively, starting with 1, the numbers being centrally located above or preferably, below, the text. The lines of the specification, and any amendments to the specification, **must be 1 1/2 or double spaced.**

II. The disclosure references application no. 08/865,341. For example, see page 20. This application has been patented. It is suggested that the disclosure be update to read Application Serial No. 08/865,341, now U.S. Patent#6,103,479.

III. The use of the trademarks has been noted in this application. See pages 71, 82, and 97, line 26 (Bodipy) for examples. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

7. Claim 1 is objected to because of the following informalities: no punctuation follows the term "comprising". It is suggested that ":" or ";" be added to the claim to obviate this rejection. See MPEP 608.01(m). Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See Fressola v. Manbeck, 36 USPQ2d 1211 (D.D.C. 1995). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation, 37 CFR 1.75(i).

8. Claim 1 is objected to because of the following informalities: Both luminescently labeled and luminescently-labeled are utilized in the claim. One phrase should be utilized for consistency. This will also clarify that the claim is directed to only one label and not two. Appropriate correction is required.

9. Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 18 is directed to a computer readable storage medium, this claim doesn't provide positive limitation to the method found in claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and
distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1 and 18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is indefinite because it is unclear in reciting "neurite outgrowth" because it is not clearly understood how one will determine what is this term encompasses. Although the disclosure defines that term as any neurite change on page 69, lines 1-3. The term/definition is a relative term, which renders the claim indefinite. The term " valid internalized cell surface receptor " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Please clarify.

B. Claim 1 is vague and indefinite because it is unclear in reciting "automatically determine" because it is not clearly understood what this limitation entails. The claim is directed to an automated method of evaluating cell surface receptor internalization in a cell, however the automated process is not clearly understood. How will the digital data be utilized to make automatic measurements? Is "automatically determine" intended to read on any automated process? As recited, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

11. Claims 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are drawn to an automated method of analyzing neurite growth. Although the claims recite several reaction parameters including an array of locations containing cells dual luminescent reporter molecules to measure location and evaluated neurons, the claims do not identify a separation step to eliminate bound and unbound materials for accurate detection and/or evaluation. There are no claimed steps reciting the washing or removal of unbound materials. If no separation will be performed it is unclear how the complex will be identified from the reaction solution containing both bound and unbound material.

Double Patenting

12. Double patenting obviousness-type rejection:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1 and 18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 52-57 and 70-91 of copending Application No. 09/398,965. This is a provisional obviousness-type double patenting rejection. Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are drawn to automated method procedures. The instant application is directed to "neurite outgrowth" as it relates to neuronal cells.

This invention is encompassed within Application No.09/398,965 wherein a cell is analyzed via the same method, specifically detecting *a luminescently labeled microtubule-labeling molecule*. Utilizing dual markers to evaluate any cell surface protein. Since the instant application is directed to "to specific cell surface protein capable of measuring neurons", it reads on the same inventive scope of Application No.09/398,965. It would have been obvious to the skilled practitioner in the art to employ various cell surface proteins, such as those found in neurite outgrowth analyzes, as they would relate to cellular evaluation in the same automated method.

This a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 1 and 18 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 40-48 of copending Application No. 09/352,171. This is a provisional obviousness-type double patenting rejection. Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are drawn to automated method procedures. The instant application is directed to "compounds that detect neurite outgrowth" as it relates to cells. This invention is encompassed within Application No.09/352,171 wherein a cell is analyzed via the same method, specifically detecting the internalization of a cell surface receptor protein (*a luminescently labeled microtubule-labeling molecule*). Neuronal cell internalization via the same method, reads on the same inventive scope of Application No.09/352,171. It would have been obvious to the skilled practitioner in the art to employ various cell surface proteins, such as those found in neuron cellular analysis, as they would relate to cellular evaluation in the same automated method.

This a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negative by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al. (Optical Diagnostics of Living Cells and Biofluids, Vol. 2678, 1996, pages 15-27) or Taylor et al. (American Scientist, 80:322-335, 1992) in view of Lee et al. (Journal of Biological Chemistry, 1995, Vol.270., No.10., pages 5600-5605) and Schroeder et al. (Journal of Biomolecular Screening, 1(2):75-80, 1996).

Taylor et al. (Optical Diagnostics of Living Cells and Biofluids) teach new technologies used in conjunction with light microscopy to measure events in living cells via an automated method.

The new automated methodology involves cell imaging and scanning techniques that are extrapolated to identify signal as digital data subsets for further analysis (multidimensional image data). See page 16, 3rd and 4th paragraphs.

Taylor et al. (American Scientist) teach new technologies used in conjunction with light microscopy to measure events in living cells. One major advance of the new methodology is found in the use of computers for digital processing and analysis of images. Another improvement is seen in the development and use of fluorescent dyes, which can be attached to specific molecular structures thereby revealing the location of those structures in the cells.

Dye molecules can also be designed so that their fluorescence is controlled by specific physiological changes; thus they indicate what is happening in the cells, as well as when and where (page 322, column 3, 1st paragraph). Taylor et. al. teach modified multi-mode light-microscope workstations that incorporate multiple electronic detectors and provide computer control of all major microscope functions. Images are converted to a digital form that can be read and manipulated by the computer (pages 324 & 325). Taylor et. al. teach indicators that reveal where a marker has gone in the cell and what conditions exist in that area, as well as the use of more than one tagging molecule with one or more suitably chosen fluorescent labels to learn whether or not the molecules are close to each other in the cell.

Taylor et al. and Taylor et al. as set forth above differ from the instant invention in not teaching an array of locations (such as a 96 well microtiter plate) or evaluations specifically directed to Neurite outgrowth analysis procedures.

Lee et al. teach metabolic labeling techniques involving protein kinetics in sympathetic neurons. Nerve growth factor-induced neurite outgrowth in PC12 cells was found to increase significantly kinesin's 32P specific activity. (See abstract)

While, Schroeder et al. teach a high throughput optical screening system for cell-base fluorescent assays. The system provides an array of locations comprising a plurality of cells in a 96-well plate, a temperature control, and is controlled by a computer in windows based software interface.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure neurite outgrowth in a cell arranged according to an array format as taught by Lee et al. and Schroeder et al. in the methods Taylor et al. and Taylor et al., to perform automated cellular event analysis with respect to a neurons, because such cell based neurite outgrowth and array (96 well plate) assays as taught by Lee et al. and Schroeder et al. were well known in the art at the time of the instant invention. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such systems, because Lee et al. taught that the labels/signals could be employed to perform subcellular analysis (organelle movement-microtubules, organelle membranes) in order to more fully understand the total mechanisms occurring in a cells physiological operations. (abstract) Schroeder et al. taught that the system reads all the wells of a standard 96-wellmicroplate simultaneously with kinetic updates in the sub-second range, thereby making it possible to record transient signals.

One having ordinary skill in the art would have been motivated to do this to acquire the enhanced sensitivity and ability to reduce background fluorescence while providing more data sets for analysis, wherein accurate and precise detection is rapidly available.

16. For reasons aforementioned, no claims are allowed.

Remarks

17. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Price et al. (USP# 5,790,710) disclose an autofocus system for obtaining measurements of fluorescent stained cellular components by scanning multiple microscope fields.

B. Harpold et al. (USP# 5,436,128) teach methods for detecting and evaluating intracellular transduction on extracellular signals.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Art Unit: 1641

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Lisa V. Cook

CM1-7B17

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7/29/01



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07/30/01